REMARKS

Amendments

Claims 39 and 51 have been amended to delete reference to predisposed hosts, and claims 40-44, 46-50, 52 and 54 are canceled. These amendments introduce no new matter.

Claim Objections

Claims 40-44 and 52-54 did limit the independent claims: a host having a tumor may or may not be determined to have the tumor; a prostate tumor may or may not be primary or metastatic; and a host-compatible cell may or may not be derived from a tumor. However, these more specific embodiments are encompassed by the pending independent claims, so claims 40-44, 46-50, 52 and 54 have been canceled as separate recitals. We note that the objection is internally inconsistent, alleging that claims 52-54 are non-limiting, while not similarly objecting to the identically worded claims 45-50. Furthermore, claims 39 and 51 are plainly not duplicates: even a cursory reading would have revealed that they recite distinct target tumor cells.

35USC112, first paragraph enablement

The unamended claims are enabled by the specification. The method is directed to inhibiting the growth of a metastatic prostate or primary mammary tumor. The method is as readily practiced on a host determined to be predisposed to the tumor as on a host determined to have the tumor. However, to expedite prosecution of the preferred embodiment, we will present the canceled subject matter in a continuing application. The pending claims are free of this rejection.

35USC112, second paragraph

Claims 40 and 52 did limit claims 39 and 51, respectively: a host having a tumor may or may not be determined to have the tumor. However, the more specific embodiments of claims 40 and 52 are encompassed by the pending independent claims, so they have been canceled as separate recitals.

35USC103(a)

Diefenbach et al. (2000, Nature Immunol. 1(2):119-26) discloses two murine ligands, H-

60 and Rae1β, as ligands for the murine NKG2D receptor. In particular, the authors report the identification of these ligands by labeled in vitro binding assays (Figs. 1 & 2) and their expression cloning (Fig. 3). The authors also used NKG2D-specific antibodies to report NKG2D expression on several cell types in vitro (Figs. 4 & 5). The authors also report that COS-7 cells (an African green monkey kidney fibroblast cell line transformed with SV-40 virus) transiently transfected to express the ligands can be stained with NKG2D, and that these NKG2D labeled cells can induce lysis and IFN production by NK cells (Fig. 6), and NO and TNF production by macrophages (Fig. 7), all in vitro.

The Action asserts that "Diefenbach also teaches detection of resultant inhibition of tumor growth..." (p.5, lines 5-6). This is a falsehood manufactured to coincide with our claim. Diefenbach discloses nothing about any tumor or any tumor inhibition. Putative ligands of the NKG2D receptor were previously identified in human cells, and Diefenbach adds to that knowledge by identifying two putative NKG2D receptor ligands in murine cells. There is nothing in Diefenbach that suggests that multivalent NKG2D reagents could be used to inhibit tumor growth. There is nothing in Diefenbach that suggests or even relates to inhibition of tumor growth. The Action misrepresents the reference.

WO 98/19167 describes immuno-detection of chimeric MICA proteins (Example 1), generation of mice transgenic in human MICA (Example 2), genetic analysis of the allelic repertoire of MICA (Example 3), and binding of T cells to cells transfected to express MICA (Example 4). There is nothing in WO 98/19167 that suggests that multivalent NKG2D reagents could be used to inhibit tumor growth.

Rather than relying on specific teachings of the reference, the Action cites the most nebulous and generic passages of WO 98/19167's abstract and summary. These passages are as particularly suggestive of the invention as any infinitely malleable Rorschach diagram, purporting to disclose every diagnostic and therapeutic use of every biomolecule made by cells (abstract; p.3, lines 13-17). The mistitled summary section purports to disclose methods for detecting cancer cells with MICA- and MICB-binding agents (p.3, line 18 - p.4, line 17; p.5, lines 13-25; p.6, lines 10-12); purifying, enriching and expanding T cells with MICA- and MICB-binding agents (p.4, line 18 - p.5, line 12; p.5, lines 26 - 32); treating patients with purified T cells (p.6, lines 1-3); increasing or decreasing MICA and MICB expression (p.6, lines 4-10, 13-15), and making transgenic animals expressing MICA (p.6, lines 16-22).

There is absolutely no more specific disclosure in WO 98/19167 teaching or suggesting how MICA or MICB or MICA- or MICB-binding agents could be used in any therapy. There is no enabling disclosure of any therapy of any kind. One skilled in the art would dismiss the broad statements of the abstract and summary for what they are: generic, nebulous, all-encompassing strategic gestures of a patent draftsperson that do not inform those skilled the art.

The Action particularly cites p. 5, lines 22-25 and p.6, lines 4-12; however, the only proposed therapeutic agents mentioned in these sections are MICA- or MICB-binding agents. Our claims do not relate to any use of MICA- or MICB-binding agents. As pointed out in our application, several distinct families of cell surface ligands for NKG2D, such as MICA and MICB have been identified. These ligands are often expressed at high levels by tumor cells, but not by normal cells in mature animals. That is why the cited art proposes use of MICA- and MICB-binding agents to target cancer cells. However, the very prevalence of these ligands on highly tumorigenic cells suggested that their presence is insufficient to provoke a host rejection of the tumor (Specification, p.1, lines 22-30), which teaches away from the presently claimed invention, wherein multivalent NKG2D ligands have been shown to provide immunotherapeutic agents to inhibit tumor growth in situ.

The Examiner is invited to call the undersigned if she would like to amend the claims to clarify the foregoing or seeks further clarification of the claim language.

We petition for and authorize charging our Deposit Account No.19-0750 all necessary extensions of time. The Commissioner is authorized to charge any fees or credit any overcharges relating to this communication to our Dep. Acct. No.19-0750 (order B01-088).

Respectfully submitted,
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